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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,987	05/30/2001	Gregory D. Plowman	038602-1180	6720

22428 7590 10/29/2003

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 10/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,987	PLOWMAN ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6 and 33-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6 and 33-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed August 21, 2003 amending the specification to delete an embedded hyperlink and/or other form of browser-executable code, canceling claims 1-5 and 7-32, amending claim 6 and adding claims 33-37 has been entered.

Claims 6 and 33-37 are pending.

Specification

The disclosure is objected to because it is unclear what "Flv" stands for in Tables 1-4. Further, the abbreviated term should be written out in full, followed by its abbreviation in parenthesis. Applicants' consideration for filing a supplemental amendment to replace "Flv" with "Fv" is noted (Remarks, page 12). The objection is maintained until an amendment is filed.

Claim Objections

Claim 6 is objected to because of the following informalities:

Claim 6 recites clause "(a)". Absent "(b)", "(a)" is not needed.

Further, claim 6 recites "TAK1" and "Ras". It is suggested that the first time an abbreviation is used in a claim that the abbreviated term be written out in full, followed by its abbreviation in parenthesis.

Appropriate correction is required.

Applicant is advised that should claim 34 be found allowable, claim 35 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 34 is drawn to a polypeptide comprising SEQ ID NO:8 and claim 34 is drawn to a polypeptide consisting essentially of SEQ ID NO:8. "Comprising" and "consisting essentially of" mean the same, i.e. both require the entire contiguous sequence of SEQ ID NO: 8 without substitutions, insertions, or deletions (although the open claim language permits additional sequences before and/or after the recited sequence).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 6 and 33-37 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

This rejection is related to the utility of SEQ ID NO:8.

Applicants disclose a human nucleic acid sequence of SEQ ID NO: 3 encoding the full length protein having the amino acid sequence of SEQ ID NO:8. The utility for SEQ ID NO:8 is based on its classification as serine/threonine phosphatase (page 54, line 8, through page 55, line 8; Table 4) and further on its classification as PP2C (Tables 1-3; page 119, line 17, through page 120, line 2). This classification is based on 89% identity over 449 amino acids with a putative *Mus musculus* protein (GenBank GI 12850332) (page 119, lines 17-19). The sequence search performed at the PTO reveals that GI 12850332 has 87.3% homology to SEQ ID NO: 8 and 74.4% homology to SEQ ID NO:3. However, GenBank GI 12850332 entry was replaced by a newer version GI 26378394 that defines the polypeptide as an unnamed protein product. The sequence search performed at the PTO did not reveal any homology between SEQ ID NO:8 and a protein for which PP2C activity was demonstrated. At most, SEQ ID NO:8 has some sequence homology to putative or probable PP2Cs which not necessarily have the PP2C activity. There is no additional data to support any function for the protein of SEQ ID NO:8.

Even accepting the plausible utility of being a PP2C, one of ordinary skill in the art would not know which type of PP2C it is. It is known in the art that at least six distinct PP2C gene products which are represent by distinct isoforms (Hanada et al. (2001) JBC, 276, 5753-5759, especially page 5753, right hand column, penultimate paragraph, cited in the specification on page 55, lines 1-2). Furthermore, the

specification does not disclose a specific function of the polypeptides of SEQ ID NO: 8, its relationship to any disease, or any specific real world use. The specification describes generic functions for the protein and nucleic acid. It appears that the main utility of the polypeptide of SEQ ID NO:8 is to carry out further research to identify the biological function and possible diseases associated with said function. Substantial utility defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utility. Thus, the claimed invention has no specific or substantial asserted utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6 and 33-37 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following rejections would apply even if the utility for a polypeptide of SEQ ID NO:8 would have been established.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6 and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 6 is drawn to a polypeptide having an amino acid sequence that is at least 90% identical to SEQ ID NO: 8 "wherein said polypeptide is involved in at least one of integrin signal transduction, the TAK1 signaling pathway, a cellular channel, a cyclin dependent kinase, and the Ras pathway". "involvement" in any process does not define the function. Therefore, the claim encompasses a genus of naturally-occurring and man made polypeptides, including phosphatases, that are widely different in function. The specification fails to provide the correlation between the structure and function common to all members of the genus.

Claim 33 is drawn to a polypeptide that comprises SEQ ID NO:8 except the polypeptide lacks one or more, but not all, of the domains of SEQ ID NO:8. Since there is no limitation on the structure of the polypeptide and the domains are not defined in terms of their structure and homology to SEQ ID NO:8, this amounts to claiming a polypeptide of any structure and function. The genus of polypeptides that comprise the above polypeptides is a large variable genus with the potentiality of exhibiting various activities. Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification does not contain any disclosure of the function of all the polypeptide sequences derived from SEQ ID NO:8. The specification discloses only a single species of the claimed genus, SEQ ID NO:8, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 6 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a PP2C of SEQ ID NO:8 (if it is shown to be PP2C), does not reasonably provide enablement for a polypeptide having an amino acid sequence that is 90% identical to SEQ ID NO:8 that is involved in various processes and has an undefined activity. It does not reasonably provide enablement for

a polypeptide of an unknown function having undisclosed homology to SEQ ID NO:8 comprising a domain of SEQ ID NO:8.The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not support the broad scope of the claims which encompass various modifications and fragments of SEQ ID NO:8 resulting in an undefined activity because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting the specific requisite activity of the polypeptide of the instant invention; (B) the general tolerance of said polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired

biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptide structure having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 33, 36 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is drawn to a polypeptide having an amino acid sequence that is at least 90% identical to SEQ ID NO: 8 "wherein said polypeptide is involved in at least one of integrin signal transduction, the TAK1 signaling pathway, a cellular channel, a cyclin dependent kinase, and the Ras pathway". "involvement" in any process does not define the function. The involvement can be due to a direct action or be indirect. Further, it is

not defined which and how cellular channel is involved, which cyclin dependent kinase is encompassed and the relationship between the claimed polypeptide and said kinase.

Claim 33 recites "N terminal domain, a C terminal catalytic domain, a catalytic domain, a C terminal domain", etc. The specification provides general discussion of said terms and does not define them in relation to SEQ ID NO:8 (page 10, line 3, through page 12, line 14). Furthermore, it is unclear what is the difference among "a C terminal catalytic domain, a catalytic domain, a C terminal domain". Therefore, without knowing which fragments of SEQ ID NO:8 are encompassed, it is impossible to know the metes and bounds of the claim.

Claims 36 and 37 recite fragments of SEQ ID NO:8 having phosphatase activity. SEQ ID NO:8 is supposed to have protein phosphatase 2C activity. It unclear whether any other phosphatase activity in addition to protein phosphatase 2C activity is implied for fragments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier et al.

Hillier et al. (1997, GenBank accession AA292266) teach a 547 bp mRNA "similar to PP2C". It has 99.8% identity to nucleotides 792-1339 of SEQ ID NO:3.

This EST is a fragment of human mRNA encoding a portion of a human protein. Therefore, it would have been obvious to one of ordinary skill in the art to use this EST to produce the encoded PP2C polypeptide. One of ordinary skill in the art would have been motivated to produce the encoded human protein in order to produce an antibody against it, for example. One of ordinary skill in the art would have a reasonable expectation of success because the mRNA was defined as "similar to PP2C". The EST of Hillier et al. renders a polypeptide that is 90% identical to SEQ ID NO:8 obvious because the claim does not require the sequence of the claimed polypeptide to be 90% identical over the entire SEQ ID NO:8. Claim 33 is obvious because the domains are not defined, *supra*, and the polypeptide encoded by the EST can be construed as comprising some domains such as, for example, C terminal domain.

Response to Arguments

Applicant's arguments filed August 21, 2003 have been fully considered but they are not persuasive.

With regard to the utility rejection applicants argue that "the specification is replete with examples of the utility of the identified phosphatases" (Remarks, page 16, emphasis added). This is not persuasive because the specification provides an overall review of protein phosphatases. Applicants further provide a table entitled "Disclosed utility for a phosphatase with sequence of SEQ ID NO:8" (page 17, emphasis added). The title of the table is somewhat misleading because the recited examples describe the utility not of SEQ ID NO:8 but of protein phosphatases in general. For example, the table entry "PP2C phosphatases are involved in at least one of integrin signal transduction, the TAK1 signaling pathway, a cellular channel, a cyclin dependent kinase, and the Ras pathway" is according to the table supported by the specification on "page 54, line 25 to page 55, line 8". However, the specification on pages 54-55 recites the prior art references related to various PP2C not to SEQ ID NO:8. Furthermore, while the claims are drawn to a polypeptide, some entries in the table are not related to a polypeptide and recite, for a example, "a substance" in "treating a disease or abnormal condition by administering a substance that modulates the activity of a polypeptide", "for recombinant production of a serine/threonine phosphatase", etc. In addition, some entries do not assert any utility and recite "can be used".

Applicants further discuss the use of the present invention in "microarray expression analysis" (page 18, 1st paragraph). This is not persuasive because this is the utility of a polynucleotide not a polypeptide, if it exists. "Applicants further relate at

page 64, lines 21-29, that "such diagnostic measure may be used for a wide range of diseases, including cancer, pathophysilogical hypoxia ..." (page 18, 2nd paragraph). In fact, at page 64, lines 21-29, the specification discloses that "due to the broad functional implications of various phosphatase families, such treatment may be effectuated to a wide range of diseases, including cancer, pathophysilogical hypoxia ..." (emphasis added), i.e. refers to general description of various phosphatases that are not necessarily PP2Cs and are definitely not SEQ ID NO:8. Thus, the specification describes the generic functions for various phosphatases. It discloses that various phosphatases can be used in diagnosis of conditions, disorders, or diseases. There is no teaching of any specific diseases or conditions associated specifically with SEQ ID NO:8.

Therefore, it appears that in the absence of any disclosed relationship between the disclosed polypeptide of SEQ ID NO:8 and any disease or disorder, the main utility of the polypeptide is to carry out further research to identify the biological function and possible diseases associated with said function. Substantial utility defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utility. In view of the above, a polypeptide of SEQ ID NO:8 is deemed as lacking utility.

Applicants further argue that "the applicants does not have to provide evidence sufficient to establish that an asserted utility "beyond a reasonable doubt". *In re* Irons,

340 F.2d 974,978,144 USPQ 351, 354 (CCPA 1965). Instead, evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true" (page 18, penultimate paragraph). For the reasons discussed above, it appears not to be the case. Applicants further argue that "a copy of an "NCBI Conserved domain Search" analysis, which classifies the amino acid sequence of SEQ ID NO:8 as a *bona fide* PP2C serine/threonine phosphatase, and shows the "significant alignment" of SEQ ID NO:8 to other serine/threonine phosphatases (page 19). This is not persuasive because Applicants did not disclose the actual alignment, overall percent identity with the given sequences and whether they represent actual PP2Cs.

With regard to the written description rejection, Applicants argue that "claim 6 is directed to an isolated, enriched, or purified polypeptide that comprises an amino acid sequence that is at least 90% identical to SEQ ID NO:8, *i.e.*, a PP2C serine/threonine phosphatase" (page 20, 2nd paragraph). Even considering SEQ ID NO:8 as a PP2C, claim 6 is not directed to a polypeptide having PP2C activity but at most as involved in certain processes. Applicants further characterize their invention as "a PP2C-related, serine/threonine phosphatase polypeptide, that functions in a particular biological pathway" (page 20, last paragraph, emphasis added). This is not persuasive because Applicants do not teach how SEQ ID NO:8 is related to PP2C and in what particular biological pathway it functions.

With regard to the enablement rejection, Applicants review the rejection but do not rebut it (page 21). However, they mention that "that conservative changes in amino acid [sequence] occur naturally or can be made in order to arrive at a protein or polypeptide which retains the functionality of the original. Thus, the present invention encompasses naturally-occurring, conservative changes in a polypeptide that render that polypeptide at least 90% identical ti SEQ ID NO:8. Alternatively, the amino acid sequence of SEQ ID NO:8 could be "modified" so as to produce a polypeptide that has a sequence that is not more that 10% different to SEQ ID NO:8" (page 22). This is not agreed with because while it is known how to produce changes in 10% of the sequence, the specification does not teach where to make theses changes without affecting the specific activity, if it is defined.

With regard to the 112, 2nd paragraph, rejection, Applicants further argue that "Depending on its length, the N-terminal domain may or may not play a regulatory role in phosphatase function" (page 22). It is considered as a support for the rejection because neither the structure nor the function of said domain is defined. Applicants further argue that "the catalytic domain can be identified following a Smith Waterman alignment" (page 22). Assuming it is correct, as the essential claimed material, said domain must be defined in the specification.

With regard to the 103(a) rejection, Applicants argue that "firstly, Hillier et al., depicts a nucleic acid cDNA clone, not an amino acid as presently recited in claim 6.

Certainly, the presently claimed isolated, enriched, or purified polypeptide of SEQ ID NO:8 does not read on such a DNA-based reference, secondly, there is no motivation or suggestion anywhere in Hillier to modify the DNA sequence, i.e., to identify the correct reading frame an produce a PP2C phosphatase family member, as the Examiner contends" (page 24). This is not agreed with because first, if Hillier et al. would teach a polypeptide, the reference would be applied as a 102 not 103 reference. Secondly, the motivation is provided by Hillier because he provides a part of the coding region of a protein "similar to PP2C". It is noted that SEQ ID NO:8 is not rejected.

Conclusion

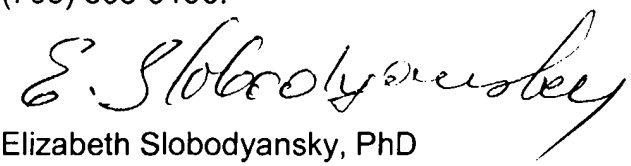
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.



Elizabeth Slobodyansky, PhD
Primary Examiner

October 22, 2003